amino acid substitution, amino acid insertion, amino acid deletion, C-terminal truncation, and N-terminal truncation, wherein upon injection into an animal the polypeptide produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5; or

(b) a nucleotide sequence complementary to the nucleotide sequence of (a);

provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22.

8. (Amended) A process of producing a polypeptide comprising the step of culturing the host cell of Claim 5 under suitable conditions to express the polypeptide encoded by said nucleic acid molecule, and optionally isolating the polypeptide from the culture, thereby producing the polypeptide.

REMARKS

In the Proposed Examiner's Amendment, transmitted by facsimile on May 9, the Examiner suggested amendments to claims 1, 3, 4, and 8, and proposed that claim 2 be canceled. The Examiner also proposed minor amendments to the specification. Applicants find the Examiner's amendments to the claims to helpful but not entirely optimal to Applicants' needs in this application, and propose that claims 1-3 and 8 be amended as indicated herein. The amendments to the claims are fully supported by the specification. No new matter has been added as a result of the above-described amendments. Applicants find the Examiner's amendments to the specification to be acceptable.

With respect to the Examiner's amendments to the claims, Applicants first contend that the Declaration Pursuant to 37 C.F.R. § 1.131, filed February 11, 2002, is sufficient to overcome the rejection of claims 2 and 3 under 35 U.S.C. § 102(a) as being anticipated by the FAPESP/LICR Human Genome Project (GenBank EST Database Accession No. AW351839). While the nucleotide sequence disclosed by the FAPESP/LICR Human Genome Project *may* have been submitted sometime in 1999 (as suggested by the entry "Unpublished (1999)" appearing at line 13 of the reference), Applicants contend that the sequence was not *accessible to the public* until February 1,

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2000 (as indicated by the entry "01-FEB-2000" appearing at line 1 of the reference), and therefore, was not *publicly known* until that date. The phrase "known or used" in 35 U.S.C. § 102(a) means "Means Publicly Known or Used." MPEP § 2132. "The statutory language 'known or used by others in this country' (35 U.S.C. § 102(a)), means knowledge or use which is accessible to the public." *Carella v. Starlight Archery*, 804 F.2d 135 (Fed. Cir. 1986). Therefore, for the purposes of antedating the FAPESP/LICR Human Genome Project, Applicants contend that the Declaration is sufficient.

Moreover, Applicants contend that the explanation of the document accompanying the Declaration sufficiently asserts a reduction to practice of the claimed invention before February 1, 2000. Specifically, paragraph 3 of the Declaration states that:

> Accompanying this Declaration is a copy of a sequence match obtained by us before February 1, 2000 documenting a reduction to practice of our invention. This match was obtained following a comparison of a nucleic acid sequence derived from the amino acid sequence of a secreted polypeptide isolated from squamous cell and colorectal carcinoma cells to a proprietary EST database.

The specification states (page 84, line 27 to page 85, line 1) that:

> Using a proteomic-based approach, a novel protein was isolated from conditioned media obtained from squamous cell and colorectal carcinoma cell lines. The approach utilized in isolating this protein suggests that it is a naturally secreted product. The amino acid sequence of the isolated protein was determined and found to share sequence identity with EST sequences present in both GenBank and proprietary (Amgen dbEST) databases.

Applicants contend that when the nucleotide sequence set forth in SEQ ID NO: 4 was obtained, the claimed invention was reduced to practice. *Amgen Inc. v. Chugai Pharmaceutical Co.*, 18 U.S.P.Q.2d 1016, 1021 (Fed. Cir. 1991). As described in the Declaration, and in the specification, that nucleotide sequence was obtained when a comparison of the amino acid sequence derived from a protein obtained from squamous cell and colorectal carcinoma cell lines was compared with a proprietary EST database. The sequence match accompanying the Declaration establishes that Applicants identified and possessed the nucleotide sequence of the claimed invention, and therefore had reduced the claimed invention to practice, before February 1, 2000.

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As the Declaration is sufficient to antedate the FAPESP/LICR Human Genome Project and establish a reduction to practice of the claimed invention, Applicants contend that the "non-naturally occurring" limitation proposed by the Examiner is not necessary to overcome the FAPESP/LICR Human Genome Project.

Regarding the rejection of claim 2 under 35 U.S.C. § 102(b) as being unpatentable under Hillier *et al.* (GenBank EST database Accession No. AA422178), Applicants contend that because the nucleotide sequence disclosed by Hillier *et al.* lacks the nucleotide found at position 258 in the nucleotide sequence of SEQ ID NO: 4 (as shown in Appendix A of Applicants' amendment filed February 11, 2002), one of ordinary skill in the art would determine that the polypeptide encoded by the nucleic acid molecule disclosed by Hillier *et al. differs* from the polypeptide set forth in SEQ ID NO: 5 at positions 77-81 and possesses an *additional* 17 amino acids at its C-terminal end. As the polypeptide encoded by the nucleic acid molecule of Hillier *et al.* is *longer* than the polypeptide set forth in SEQ ID NO: 5, Applicants contend that the nucleic acid molecule of Hillier *et al.* cannot anticipate a nucleic acid molecule that encodes a polypeptide fragment of at least about 25 amino acid residues of the polypeptide set forth in SEQ ID NO: 5. In other words, the genus of variants defined by claim 2 (in which the largest member of the genus must encode a polypeptide of no more than 80 amino acids) does not encompass the nucleic acid molecule of Hillier *et al.* (which would encode a polypeptide of 98 amino acids).

For the reasons provided above, Applicants also contend that the Examiner's proposed deletion of "C-terminal truncation" variants from claim 3 is not necessary to overcome the Hillier *et al* reference. However, to distinguish the nucleic acid molecules of claim 3 from the nucleic acid molecule of Hillier *et al.*, Applicants have added the limitation "provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22" (wherein the amino acid sequence of SEQ ID NO: 22 is E-S-H-R-C-S-T-P-K-A-R-L-Q-T-A-E-N-L-M-P-G-T), thereby excluding nucleic acid molecules that encode a C-terminal sequence that would be identical to C-terminal sequence of the polypeptide encoded by the nucleic acid molecule of Hillier *et al.*

Finally, in response to the Examiner's proposed cancellation of claim 2 and deletion of subpart (b) from claim 1, Applicants have amended claims 1 and 2 to recite "the nucleotide sequence

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of the DNA insert in ATCC Deposit No. PTA-1755, wherein the DNA insert encodes: (i) the polypeptide as set forth in SEQ ID NO: 5, or (ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution." Applicants contend that the amendment overcomes the rejection of claims 1 and 2 under 35 U.S.C. § 112, second paragraph, and that claims 1 and 2 are no longer indefinite, since the sequence inherently encoded by the deposited DNA insert is explicitly recited in the specification, and the amendments establish the nexus between the deposited insert and the disclosed sequence.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited. If Examiner Rawlings believes it to be helpful, he is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: May 17, 2002

By: _____
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AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Twice Amended) An isolated nucleic acid molecule comprising:

(a) the nucleotide sequence as set forth in SEQ ID NO: 4;

(b) the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755, wherein the DNA insert encodes:

(i) the polypeptide as set forth in SEQ ID NO: 5, or

(ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution;

(c) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 5; or

(d) a nucleotide sequence complementary to any of (a) - (c).

2. (Twice Amended) An isolated nucleic acid molecule comprising a region of the nucleotide sequence of:

(a) SEQ ID NO: 4, or

(b) the DNA insert in ATCC Deposit No. PTA-1755, wherein the DNA insert encodes:

(i) the polypeptide as set forth in SEQ ID NO: 5, or

(ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution;

encoding a polypeptide fragment of at least about 25 amino acid residues wherein upon injection into an animal the polypeptide fragment ~~has an activity of the encoded~~ produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5, ~~or is antigenic~~.

3. (Twice Amended) An isolated nucleic acid molecule comprising:

(a) a nucleotide sequence encoding a polypeptide, that is the polypeptide as set forth in SEQ ID NO: 5 but with at least one modification thereof ~~that is~~ selected from the group consisting of an ~~conservative~~ amino acid substitution, amino acid insertion, amino acid deletion, C-terminal

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truncation, ~~or~~ and N-terminal truncation, wherein upon injection into an animal the ~~encoded~~ polypeptide ~~has an activity of~~ produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5; or

(b) a nucleotide sequence complementary to the nucleotide sequence of (a);

provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22.

8. (Amended) A process of producing a ~~Secs 1~~ polypeptide comprising the step of culturing the host cell of Claim 5 under suitable conditions to express the polypeptide encoded by said nucleic acid molecule, and optionally isolating the polypeptide from the culture, thereby producing the polypeptide.

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PENDING CLAIMS

Clean Versions of Pending Claims under 37 C.F.R. 1.121(c)(3)

1. An isolated nucleic acid molecule comprising:

(a) the nucleotide sequence as set forth in SEQ ID NO: 4;

(b) the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755, wherein the DNA insert encodes:

(i) the polypeptide as set forth in SEQ ID NO: 5, or

(ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution;

(c) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 5; or

(d) a nucleotide sequence complementary to any of (a) - (c).

2. An isolated nucleic acid molecule comprising a region of the nucleotide sequence of:

(a) SEQ ID NO: 4, or

(b) the DNA insert in ATCC Deposit No. PTA-1755, wherein the DNA insert encodes:

(i) the polypeptide as set forth in SEQ ID NO: 5, or

(ii) the polypeptide as set forth in SEQ ID NO: 5 but with at least one amino acid substitution;

encoding a polypeptide fragment of at least about 25 amino acid residues wherein upon injection into an animal the polypeptide fragment produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5.

3. An isolated nucleic acid molecule comprising:

(a) a nucleotide sequence encoding a polypeptide, that is the polypeptide as set forth in SEQ ID NO: 5 but with at least one modification thereof selected from the group consisting of an amino acid substitution, amino acid insertion, amino acid deletion, C-terminal truncation, and N-

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terminal truncation, wherein upon injection into an animal the polypeptide produces an antibody that binds to the polypeptide as set forth in SEQ ID NO: 5; or

(b) a nucleotide sequence complementary to the nucleotide sequence of (a);

provided that the encoded polypeptide does not further comprise the amino acid sequence of SEQ ID NO: 22.

4. A vector comprising the nucleic acid molecule of Claims 1, 2, or 3.

5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing a polypeptide comprising the step of culturing the host cell of Claim 5 under suitable conditions to express the polypeptide encoded by said nucleic acid molecule, and optionally isolating the polypeptide from the culture, thereby producing the polypeptide.

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